SUBJECT: Abbreviated Risk Assessment for J15-31 FROM: Gwendolyn McClung, Ph.D. Technical Integrator Assessment Branch 3 Risk Assessment Division (7403M) TO: Jesse Miller, Ph.D. Program Manager New Chemicals Notice Manufacture Branch Chemical Control Division (7405M) THRU: Cathy Fehrenbacher, CIH Chief Assessment Branch 3 Risk Assessment Division (7403M) Iris Camacho, Ph.D. Acting Branch Chief Assessment Branch 2 Risk Assessment Division (7403) DATE: July 30, 2015 SUMMARY There is low risk associated with the use of the intergeneric

There is low risk associated with the use of the intergeneric as there are low potential hazards to human health and the environment from the microorganism and low exposures to workers, the general population, and the environment with this closed system fermentation. The parental microorganism has a long history of safe use and the genetic modifications which consist of the introduction of

human health or ecological hazards.

I. INTRODUCTION

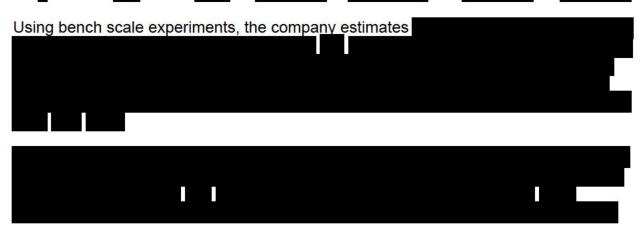
The Agency has received a Microbial Commercial Activity Notice (MCAN) from Danisco US, Inc. (operating as DuPont Industrial Biosciences) for an intergeneric Saccharomyces cerevisiae strain that has

a previous submission	the recipient S. cerevisiae strain was modified by the
introduction of a	
	. In the current
submission, a	
400	resulting in the new submission strain . The parental
strain is S. cerevisiae	
	The genetic modifications
allows for	that can then be fermented into ethanol
by the microorganism. Th	e production microorganism, strain will thus be used for
production of fuel ethanol	rom grain.
Although S. cerevisiae is of	ne of the ten microorganisms eligible for the 5(h)4 Tiered
The state of the s	eporting, the company has chosen to submit this strain for an
MCAN review because	

II. PRODUCTION VOLUME

The proposed production volumes for years 1, 2, and 3 are given in the following table.

Year	# of	Dry Cell	Total Dry	Total Wet	Total Wet	Total
	Batches	Weight	Cell Mass	Cell Mass	Cell	Active
		(kg) per	(kg)	Fermentation	Mass	Dry Yeast
		Batch	5 37.0	Broth (kg)	Concentrated	Product
					Cream (kg)	(kg)



III. TAXONOMY

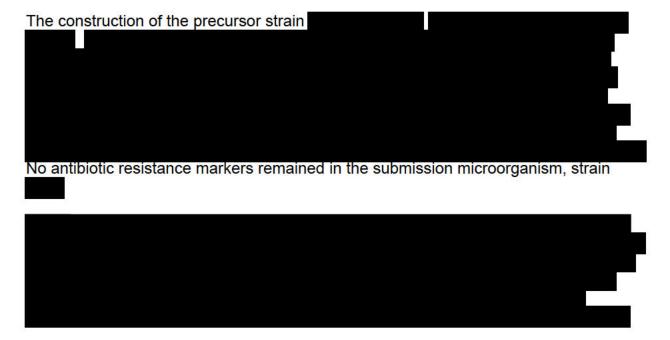
The recipient microorganism is Saccharomyces cerevisiae strain, data on 18S rDNA sequencing performed by the company was submitted to confirm the identity as S. cerevisiae. The identity of the parental strain is accepted as being S. cerevisiae (Segal, 2015b).

IV. HISTORY OF SAFE USE

Saccharomyces cerevisiae has an extensive history of safe use in the area of food processing. Also known as baker's yeast or brewer's yeast, this organism has been used for centuries as a leavening for bread and as a fermenter of alcoholic beverages. The risk assessment of *S. cerevisiae* for the 5(h)(4) Tiered Exemptions Final Risk Assessment for *S. cerevisiae* (http://www.epa.gov/opt/biotech/pubs/pdf/fra002.pdf) concluded that this yeast presents low hazards to human health and to the environment. EPA has reviewed this recipient microorganism in a number of recent MCANs:

V. CONSTRUCT ANALYSIS

A. Construction of the Submission Microorganism



All of the modifications were performed in such a way that no bacterial vector sequences remain in the submission strain. No introduced antibiotic resistance markers remain in the submission. This was verified by characterization of the strain by Southern blot analyses and polymerase chain reaction (PCR).

The genetic modifications enable the submission strain to Wild-type *S. cerevisiae* does not

B. Potential Hazards of the Genetic Modifications

There is low hazard associated with the introduced submission strain of	gene to create the . The introduced
have a long history of safe use in the food	industry. is
common in microorganisms and merely enables the produc	ction organism to convert
which can then be fermented into ethanol	•
There is low hazard associated with the introduced	
and is also found in humans and of	ther mammals. The donor
microorganism, is ubiquitous in the environment	
vegetation. It has a long history of safe use for	,,

The introduced genes were both stably inserted into the chromosome which means they are unlikely to horizontally transfer to other microorganisms in the environment if the submission microorganism was inadvertently released from the manufacturing facility or ethanol production plants. There is low concern for horizontal gene transfer, and there would be low concern even if the genes were to be transferred.

VI. HUMAN HEALTH HAZARDS

The concern for human health effects associated with the recipient microorganism is low (Ward, 2015). The recipient strain for the MCAN submission is *Saccharomyces cerevisiae* which has extensive history of safe use. *Saccharomyces cerevisiae* is non-pathogenic and non-toxic.

The introduced genetic material also does not present health-related concerns.

. Since the company uses personal protective equipment (lab coats, safety glasses, latex or nitrile gloves, uniforms, and respirators) during manufacturer, there is low concern for exposure and allergy due to the submission microorganism.

Since there are no introduced antibiotic resistance markers in the final organism, there is low concern for antibiotic resistance genes spreading in the environment.

VII. ECOLOGICAL HAZARDS

There are low ecological hazard concerns for the recipient microorganism, *S. cerevisiae* (Muneer, 2015). The recipient microorganism does not pose any pathogenicity/toxicity concerns to plants or animals. It is a benign yeast that is ubiquitous in the environment. The risk assessment of *S. cerevisiae* for the 5(h)4 Tiered Exemption stated that there are low ecological hazards associated with this microorganism.

The introduced genes do not pose any concerns for pathogenicity/toxicity of the submission microorganism. It merely enables the yeast, , thus enabling its use on grains in ethanol production. Although the strain may survive if inadvertently released into the environment, there would be no ecological concerns (Muneer, 2015).

VIII. INTEGRATED RISK ASSESSMENT

There is low risk to human health and the environn	nent associated with the production of
and use of	containing the intergeneric genes
encoding	. The recipient microorganism is
not pathogenic to humans, other animals, or to pla	ints. It has a long history of safe use
and is ubiquitous in the environment. The	s are
common in many microorganisms and do not pose	e human health or ecological
concerns.	
which is subsequently fermented into ethanol. The	BELT :
chromosome which reduces the potential for horizon	
microorganisms were inadvertently released in the	
vector sequences remaining in the production micr	roorganism. The production
microorganism does not contain any introduced an	ntibiotic resistance marker genes.
Thus, there is low risk to human health and the env	vironment with the manufacture and
use of this Saccharomyces cerevisiae strain	

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